

## Legend of Supplemental Figure

### Supplemental Figure 1

*IER3 distribution in PDAC tissue from Mist1; Kras<sup>G12D</sup>; Trp53<sup>+/-</sup> mice.* Immunohistochemistry of IER3 and Hematoxylin-Eosin (H&E) in pancreas tissue from *Mist1; Kras<sup>G12D</sup>; Trp53<sup>+/-</sup>* mice. Strong IER3 staining is observed in cancerous ductal-like structure (upper panels) and in ADM and peritumoral acini (middle panels). Faintly or no staining is observed in sane tissue from the same samples.

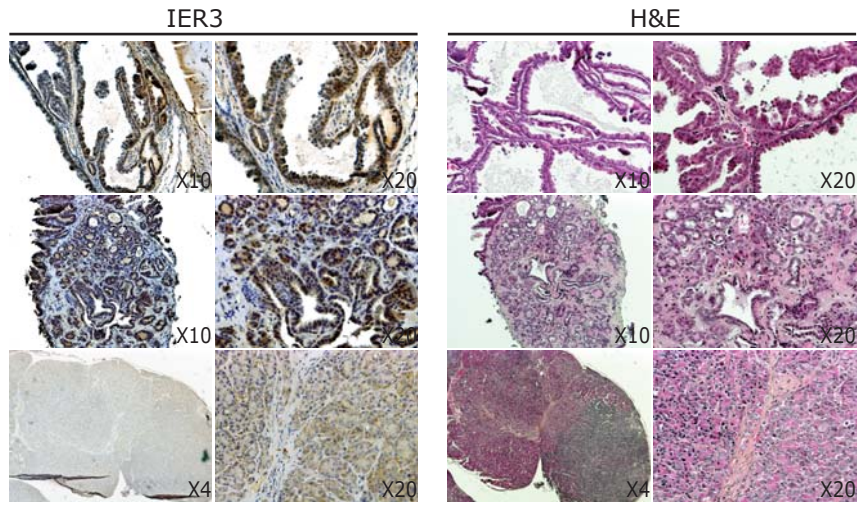
### Supplemental Figure 2

*IER3 maintains ERK1/2 phosphorylation through PP2A-B56 inhibition.* Human pancreatic cancer cells lines were treated for 48h with specific siRNA. DNA plasmid transfections were made 24 hours before samples evaluation. (A) Efficiency of siRNA against IER3 was evaluated in MiaPaCa2 and Panc1 cells by qPCR and western blot. (B) Western blots in MiaPaca2 and Panc1 cells lysates after siRNA treatment against IER3 or with a scrambled siRNA used as control. (C-D) p-ERK1/2 was evaluated by immunofluorescence and by flow cytometry in MiaPaCa2 cells. (E-F) Western blots in MiaPaCa2 transfected with HA-IER3 (IER3 wild type), HA-IER3(T18A) and HA-ΔBD-IER3, B56 (PP2A's B56β subunit) expression plasmids. Additionally, cells were transfected with a plasmid expressing a shRNA against B56β subunit. (G) ERK1/2 phosphorylation was evaluated by western blot in MiaPaCa2 cells. Cells were treated with specific siRNA against NUPR1, RELB or IER3. The quantification in western blot represents the average of four independent experiments.

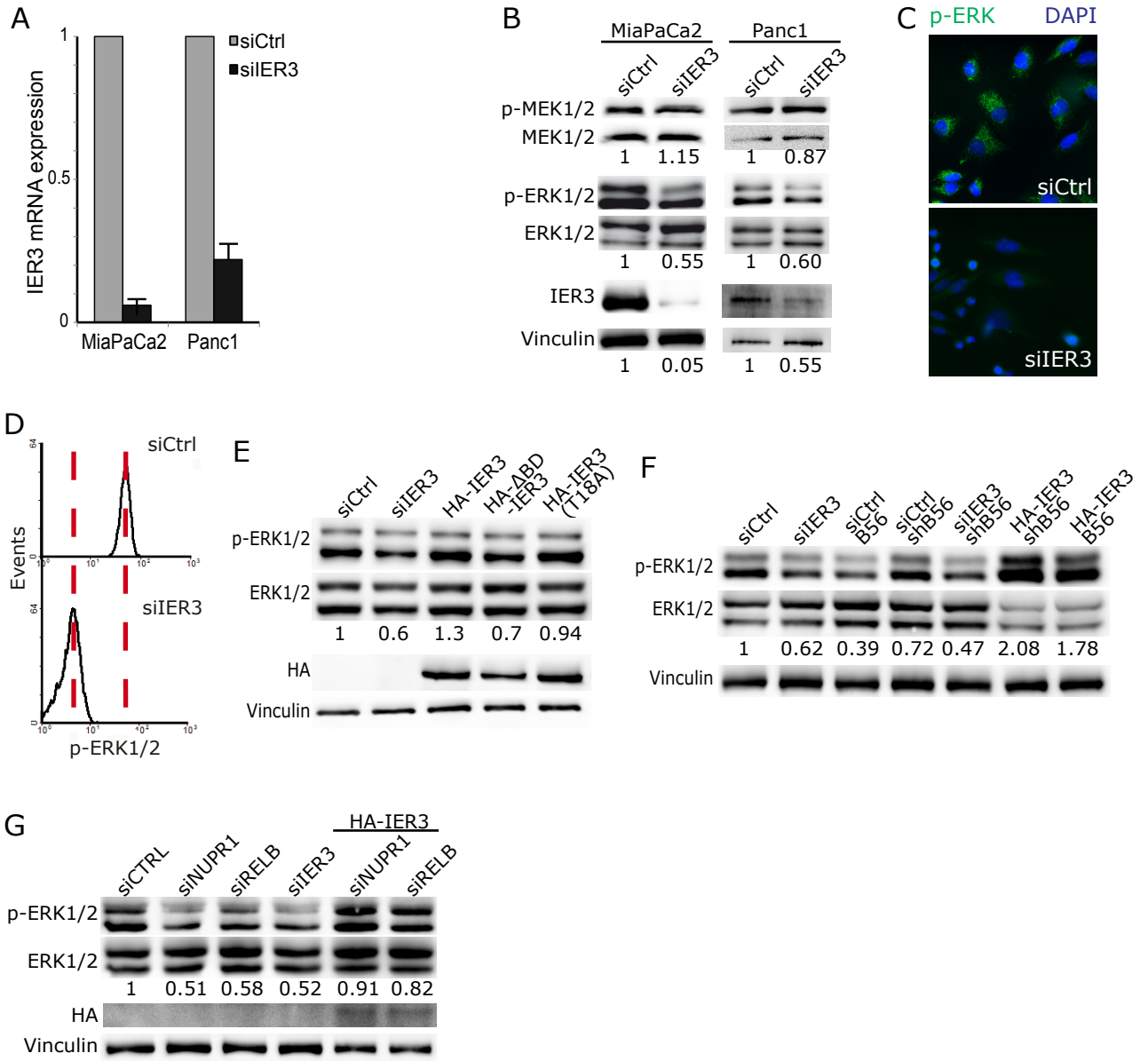
### Supplemental Figure 3

*Tumor growth of pancreatic cancer cells after IER3 mutants tranfections.* (A) The primary CKΔI-1 and CKΔI-2 cells were transfected with plasmids encoding for HA-IER3, HA-IER3-ΔBD, HA-IER3-T18A, ERK2-L73P/S151D, shIER3 or with an empty vector and implanted subcutaneously in 3 to 5 male nude mice. Tumor size was measured once weekly. p-ERK1/2 was evaluated by Western blots in CKΔI-1 and CKΔI-2 cells lysates. (B) MiaPaCa2 and Panc1 cells were transfected with shIRE3 or shScramble and implanted subcutaneously in 5 male nude mice. Tumor size was measured once weekly.

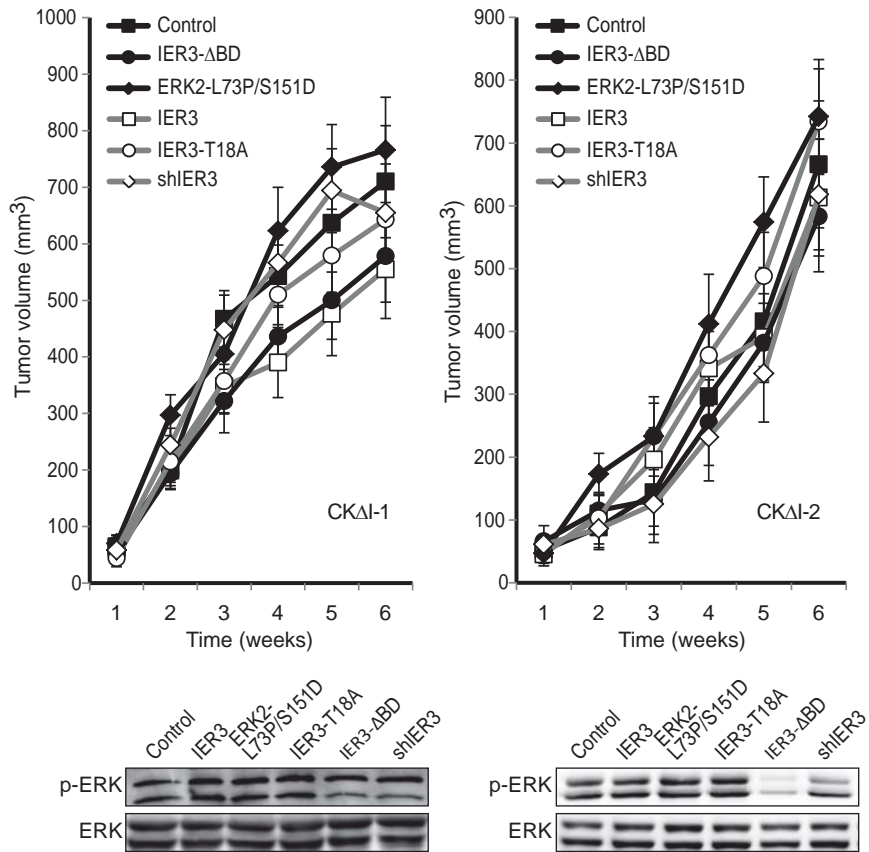
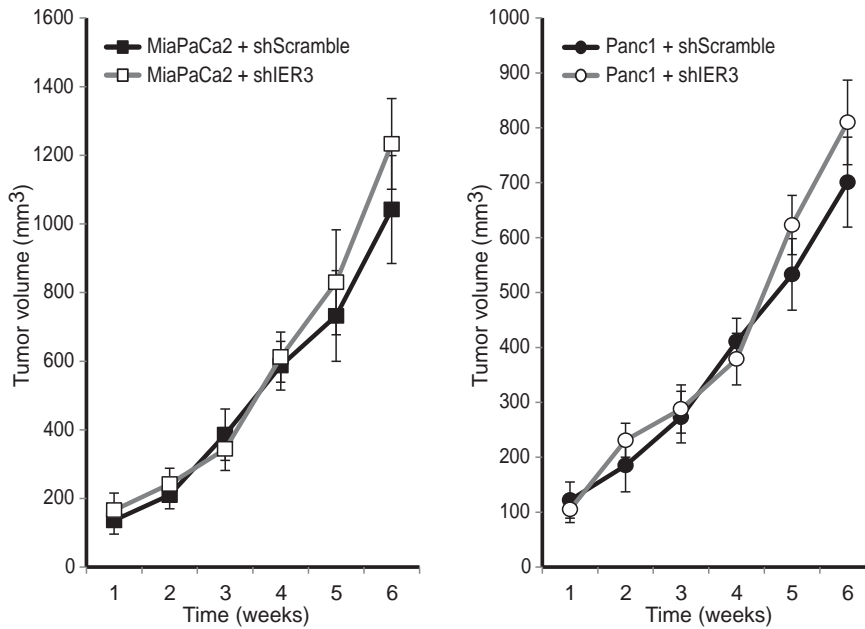
Mist1; Kras<sup>G12D</sup>; Trp53<sup>+/-</sup> mice pancreas tissue



Supplemental Figure 1



Supplemental Figure 2

**A****B**

Supplemental Figure 3